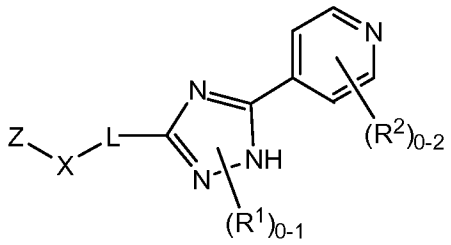
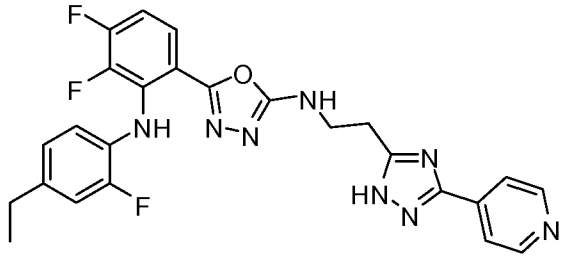
REMARKS

New claims 55-67 have been added. These claims correspond to claims 6-18 except that the structure,



has been omitted. Accordingly, these new claims present no new subject matter.

Claims 1-3 were rejected as anticipated under 35 U.S.C. § 102(e) by Biwersi *et al.* for disclosure of the compound of Example 136:



{5-[2-(4-Ethyl-2-fluoro-phenylamino)-3,4-difluoro-phenyl]-1,3,4-oxadiazol-2-yl}-[2-(5-pyridin-4-yl-2H-1, 2, 4-triazol-3-yl)-ethyl]-amine

Without acquiescing to the assertion that Biwersi *et al.* is properly prior art under 102(e) or anticipates the present claims, claim 1 has been amended by deleting H from the definition of R^3.

In view of the foregoing, Biwersi *et al.* does not anticipate the claims.

Nor does Biwersi *et al.* render the present claims obvious. None of the compounds of Biwersi *et al.* are within the scope of the compounds recited in the present claims. And there are no teachings suggesting modifying the compounds disclosed therein in a manner that would yield the compounds recited in the present claims.

The Office Action contends that the compounds recited in the present claims are obvious homologs of those of Biwersi and differing only by a single methylene moiety. But the Office

Action does not identify any compound other than that of Example 136, which is now excluded from the scope of the claims.

In cases involving new chemical compounds, it is necessary to "identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.* 492 F.3d 1350, 1357 (Fed. Cir. 2007). *See also Procter & Gamble Co. v. Teva Pharma. USA, Inc.,* 566 F.3d 989, 994 (Fed. Cir. 2009). Inherent in modification of a known compound is a reasoned identification of the known compound. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.,* 533 F.3d 1353, 1359 (Fed. Cir. 2008) ("...post-KSR, a *prima facie* case of obviousness for a chemical compound still, in general, begins with a reasoned identification of a lead compound.")

The Office has provided no basis in Biwersi for selecting Example 136 to compare to the present claims. And the applicants submit that there is nothing in Biwersi that distinguishes the compound of Example 136 in any manner that would bring it to the attention of one of ordinary skill in the art, much less suggest it for modification in any manner, let alone in a manner that would lead to the compounds recited in the present claims. Structural similarity of prior art compounds with claimed compounds is, by itself, insufficient.

"[P]roof of obviousness based on structural similarity requires clear and convincing evidence that a medicinal chemist of ordinary skill would have been motivated to select and then to modify a prior art compound (e.g., a lead compound) to arrive at a claimed compound with a reasonable expectation that the new compound would have similar or improved properties compared with the old." *Daiichi Sankyo Co. v. Matrix Laboratories Ltd.*, 619 F.3d 1346, 1352 (Fed. Cir. 2010*)*. Inherent in modification of a known compound is a *reasoned identification* of the known compound. *Eisai*, 533 F.3d at 1359 (emphasis added) ("...post-KSR, a *prima facie* case of obviousness for a chemical compound still, in general, begins with a *reasoned identification* of a lead compound.")

"[I]t is the possession of promising useful properties in a lead compound that motivates a chemist to make structurally similar compounds. Yet the attribution of a compound as a lead compound after the fact must avoid hindsight bias; it must look at the state of the art at the time the invention was made to find a motivation to select and then modify a lead compound to arrive at the claimed invention." *See Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364, 86 USPQ2d 1196 (Fed. Cir. 2008). Accordingly, proving a reason to select a compound as

a lead compound depends on more than just structural similarity, but also knowledge in the art of the functional properties and limitations of the prior art compounds. *See Eli Lilly*, 471 F.3d at 1377-79. "Potent and promising activity in the prior art trumps mere structural relationships." *Daichii Sankyo*, 96 USPQ2d at 1532.

Once a lead compound has been selected, there must be a motivation for a medicinal chemist to modify the compound to obtain the claimed compounds. "It remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda*, 492 F.3d 1350, 1357, 83 USPQ2d 1169 (Fed. Cir. 2007), *cited in Procter & Gamble Co. v. Teva Pharmaceuticals USA Inc.*, 566 F.3d 989, 90 USPQ2d 1947 (Fed. Cir. 2009).

The applicants respectfully submit that the Office has failed to satisfy at least the first two bases for establishing obviousness: (1) it has failed to identify a lead compound that is suggested by the prior art itself as opposed to through hindsight structural similarity to the claimed compounds and (2) it has failed to demonstrate a basis why one of ordinary skill in the art would have reason to modify such a compound.[1]

In view of the forgoing, therefore, the applicants respectfully request withdrawal of the obviousness rejection.

If there are any questions or comments regarding this application, the Examiner is encouraged to contact the undersigned in order to expedite prosecution.

Respectfully submitted,

Date: August 4, 2011

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[1] Because the first two prongs of the obviousness analysis have not been satisfied, the applicants do not address the third prong, demonstrating that the claimed compounds would be reasonably predicted to have the properties observed, because it is unnecessary. But in so doing, the applicants make no admission regarding it.